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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,014	02/19/2004	Selena Chan	42P14581	4300

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EXAMINER

MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/782,014	<b>Applicant(s)</b> CHAN ET AL.	
	<b>Examiner</b> Marjorie A. Moran	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 February 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Election/Restrictions***

Applicant's election of Group I and species of complex organic-inorganic nanoparticles, and of optical device in the reply filed on 9/13/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). An action on the merits of pending claims 1-24 follows.

***Drawings***

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: time maps 310, 320, 33, and 340 are not shown in Figures 2, 4, or 5, as described on page 3, lines 25-32 and page 4, lines 10-14.. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> para***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 7, and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a LACK OF WRITTEN DESCRIPTION rejection.

Complex organic-inorganic nanoparticles which may be used as bulky group labels, as recited in claims 5 and 17, or used to separate monomers, as recited in claim 7, are not described by the instant specification such that one skilled in the art would know what structures were contemplated by applicants for use in the claimed methods at the time of filing of the instant application. The instant specification discloses, on page 13, lines 11-12, that one example of nanoparticles which may generate "unique optical signals" are complex organic-inorganic nanoparticles (COINs) "that are currently under development." Lines 14-25 on page 13 disclose metal groups and cross-linked nanoparticles, but do not disclose whether these are COINs or are simply another type of nanoparticle which maybe used as labels. It is noted that cross-linked nanoparticles maybe entirely organic or entirely inorganic, and that nanoparticles comprising metal may be entirely inorganic, thus a statement that cross-linked and metal nanoparticles

Art Unit: 1631

are described in the prior art is not a description for COINs intended for use in the inventive/claimed methods. Nowhere does the instant specification fully describe or exemplify COINs such that one skilled in the art would know what structures or chemical entities were envisioned by applicants for use in the claimed methods. For these reasons, claims 5, 7, and 17 lack a full and complete written description, and are rejected.

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

A method of use of monomers which are partially labeled such that the average time (of cleavage/detection?) between two labeled monomers is "significantly different" from the average time (of cleavage/detection?) of two unlabeled monomers, wherein the unlabeled monomers are the same type as the labeled monomers, is not enabled as neither the instant specification nor the prior art teach how to make and use monomers with such properties.

It is unclear what limitation is intended, as set forth below; however, the examiner has attempted to interpret the claims in light of the teachings of the specification, as follows.. The instant specification teaches several methods of labeling monomers, including cross-linking (pages 14-15) to nanoparticles or antibodies, and

Art Unit: 1631

polymerization/incorporation of labeled nucleotide "precursors" (page 11). The specification further teaches on page 11 that use of a "lower percentage" of labeled nucleotide precursors results in "signal stretching." However, it is commonly known in the art that adjacent nucleotides in a polynucleotide chain have a fairly uniform spacing (or distance) regulated by the structure of the bonds between nucleotides. Adding labels to a previously formed polynucleotide would not affect the bond distance between two nucleotides in the chain. In a polymerization reaction, use of a "precursor" which affects the bond distance would be expected to result in a precursor which does NOT become incorporated, as the bond would not form, or would be expected to terminate polymerization, again, due to irregular bond formation, and thus would result in a polymer wherein no two adjacent nucleotides are labeled. The prior art is silent with regard to how to make a partially labeled monomer or polymer wherein the time of cleavage/distance between adjacent monomers with labels is "significantly" different or longer than the time of cleavage/distance between similar adjacent monomers which are unlabeled.

As neither the instant specification nor the prior art teach how to make partially labeled monomers with the claimed properties, the claims are not enabled.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> para***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 recite "different monomer types comprising a polymer," each in step (a). Those of skill in the art generally define a monomer as a single unit which can combine or polymerize with other monomers to FORM a polymer. By definition, a polymer is comprised of monomers. As those skilled in the art do not usually consider a monomer as a unit which comprises polymers, it is unclear what is intended by a monomer types "comprising a polymer," therefore the claims are indefinite. If applicant intends monomer types "comprised within" the polymer or a similar limitation, then clarification through clearer claim language is requested.

Claim 1 and 13 limit a polymer to comprise monomer subtypes which are partially labeled such that an "average time between two adjacent labeled monomers is significantly larger than an average time between two adjacent monomers of the same type" which is generally confusing for the following reasons:

First, it is unclear what "average times" are intended; i.e. average time of separation (e.g. on a gel or through a column), average time of detection, average time of labeling, average time of decay of the labels attached to the monomers, etc.

Second, it is unclear what is intended by "two adjacent labeled monomers" versus "two adjacent monomers of the same type." The claims recite "only one of the monomer types ... is partially labeled", therefore all labeled monomers are of the "same type." As all labeled monomers are of the same type, then all "adjacent labeled monomers" are the same as "adjacent monomers of the same type," and the claim is both indefinite and not enabled. It is noted that any two adjacent monomers of the "same type" will be the same distance apart in a polymer regardless of labeling, therefore it is unclear how the distance between adjacent labeled monomers is to be different from the time between two adjacent UNLABELED monomers (of the same type as the labeled monomers). See the lack of enablement rejection above.

Third, it is unclear what is intended to be of the "same type." As indicated above, one interpretation is that the monomers are to be of the "same type." However, an alternate interpretation is that the LABELS are to be of the "same type" wherein the monomers may or may not be different.

As the limitation(s) intended by the phrases set forth above are unclear, the claims are indefinite.

The term "significantly larger" in claims 1 and 13 is a relative term which renders the claims indefinite. The term "significantly" with regard to "larger" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. As one skilled in the art would not know how much larger an "average time" must be to be "significantly larger," the claims are indefinite.



Art Unit: 1631

Claims 1 and 13 recite the phrase "before labelling" in the last line of step (a). It is unclear what is intended to occur "before labelling" therefore the claims are indefinite.

Claims 6 and 18 recite the limitation "the labeled nucleic acid strand," each in lines 1-2. There is insufficient antecedent basis for this limitation in the claims, therefore the claims are indefinite. Parent claims 2 and 14 limit a polymer to be a nucleic acid, but do not recite either a nucleic acid "strand" nor a "labeled" nucleic acid.

Claim 7 limits sequentially separating each monomer to be "done by an enzyme and complex organic-inorganic nanoparticles." It is unclear whether separation is to be "done" or accomplished with both an enzyme and the complex particles, or whether the enzyme is to perform the separation while the complex particles "do" something else. It is noted that complex nanoparticles, generally, are not known in the art to have enzymatic activity or separation properties, nor are such nanoparticles described by the instant specification, therefore claim 7 maybe neither enabled nor fully described by the instant specification. However, as the limitation intended is unclear, the claims are rejected herein only for indefiniteness. If applicant intends to limit the separation to comprise cleavage by an enzyme and separation based on size (or other properties) of the bulky groups, then this is not reflected in the claim. Clarification of the step(s) and limitations intended is requested.

Claim 8 recites "wherein polymer is a nucleic acid" in line 1. It is unclear whether applicant intends --the polymer-- or --a polymer--. If the former, then it is unclear what further limitation of the polymer is intended by limiting it to be a nucleic acid, as parent claim 2 previously limited the polymer to be a nucleic acid. If the latter, then it is unclear

Art Unit: 1631

whether applicant intends the same polymer as parent claims 1 and 2, or a different polymer.

Claim 24 limits at least one end of "each nucleic acid to be attached to a distinguishable label. However, parent claim 13 does not recite a nucleic acid, therefore it is unclear what further limitation of parent claim 13 is intended.

### ***Conclusion***

No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Monday-Friday; 6 am-2:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1631

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marjorie A. Moran  
Primary Examiner  
Art Unit 1631



11/27/06